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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,452	07/13/2001	Mohammad Sarwar Nasir	01-660	5761

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EXAMINER	
DAVIS, DEBORAH A	

ART UNIT	PAPER NUMBER
1641	12

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/905,452	NASIR ET AL.	
	Examiner	Art Unit	
	Deborah A Davis	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's arguments response to the Office Action mailed July 07, 2003 (Paper #7) is acknowledged. Currently, claims 1-18 are pending and under consideration.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-4 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nasir et al (Combinatorial Chemistry & High Throughput Screening, 1999, 2, 177-190) in view of Dixon et al (USP#4,835,100) and further in view of Dhar et al (US Pub 2002/0110803).

Nasir et al teaches field tests to determine mycotoxins in human, animal and grain diseases. (pg. 18, last para.). Nasir et al teaches a homogenous assay using fluorescence polarization to analyze these mycotoxins in grains (See abstract). Mycotoxins that are extracted from grains, with a suitable solvent and the sample are added into the antibody solution. A mycotoxin antigen of interest is labeled with a fluorescent molecule (tracer) and is added to the antibody solution. Once the reaction takes place, the fluorescent polarization of the tracer is then measured (pg. 182, para. 1). Nassir et al also teaches that using fluorescent polarization assays has good sensitivity and the possibility of obtaining results rapidly without any separation and

purification steps make fluorescent polarization more attractive than methods where one needs to physically separate the bound and unbound species before analysis.

Nasir et al does not point out if the particular mycotoxin used was an alfatoxin neither does he make reference to the particular solvent used to extract mycotoxins from a sample.

However, Dixon et al teaches a method and a test kit for detecting an aflatoxin B1 using monoclonal antibodies (See abstract). Dixon et al explains that aflatoxins are toxic metabolites and they can act as potent carcinogens, mutagens and teratogens and are known to occur naturally in wheat and other foods (col. 1, lines25-34) and (col. 10, lines 45-52). Dixon et al uses methanol as an extraction solvent (col. 11, lines 36-47).

Dixon et al does not teach conjugation of an aflatoxin B1-O-carboxymethyl oxime being conjugated to a flourophore.

However, Dhar et al teaches a conventional assay for afltoxin B1 where aflatoxin B1-O-carboxymethyl oxime is conjugated to Horseradish peroxidase (page 9, paragraph 0102).

It would have been obvious to one of ordinary skill in the art to use the method of detecting alfatoxins B1 in food as taught by Dixon et al into the assay of Nasir et al for detecting mycotoxins, to detect toxic levels of contamination in food. It would have been obvious for Nasir et al to want to detect alfatoxins in grain because certain levels are a public health risk because of the health hazard that they pose to humans and animals. Although Dhar et al does not teach aflatoxin B1-O-carboxymethyl oxime conjugated to a fluorophore, it would have been obvious to one of ordinary skill in the art

to substitute the Horseradish peroxidase label for a fluorophore and use it in the Flourescent Polarization assay taught by Nasser et al because this type of assay is sensitive and results can be obtained rapidly without any separation and purification steps. The use of methanol for an extraction solvent is an obvious equivalent of the suitable solvent taught by Nasir et al. With respect to measuring the fluorescence polarization and comparing it with known concentrations of aflatoxin, it would have been obvious to one skilled in the art to compare toxic levels of aflatoxin in grain to known concentrations in order to determine if said aflatoxins are at high enough levels to pose a health risk.

4. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nasir et al, in view of Dixon et al and further in view of Dhar et al as applied to claims 1-4 and 8 and further in view of Michel et al (USP#5,741,654).

The teachings of Nasir et al, Dixon et al and Dhar et al are set forth above and differ from the instant claims in not particularly pointing out a particular type of fluorescein used in the assay.

However, Michel et al discloses a Fluorescence Polarization assay for the quantification of antibodies in which a variety of fluoresceins are used as detectable moiety components of tracers, such as one mentioned in particular, the 6-aminofluorescein moiety (isomer II of fluorescein) which is one of the preferred moieties of choice in the said assay (col. 8, lines 1-22).

It would have been obvious to one of ordinary skill in the art to employ a fluoresceinamine or its isomers as binding moieties because such structures are well known in the art to work well in Fluorescence Polarization Immunoassays for quantitation of a sample. In addition, the fluorescein used for labeling in this assay would have been a functional equivalent of the fluorescent molecule used for labeling in the assay of Nasir et al - wherein both would have worked equally as well.

5. Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nasir et al in view of Dixon et al, and further in view of Dhar et al as applied in claims 1-4 and 8 and further in view of McMahon et al (USP#5,166,078).

The teachings of Nasir et al, Dixon et al and Dhar et al are set forth above and differ from the instant claims in not teaching the construction of a standard curve using a plurality of different known concentrations of aflatoxin.

However, McMahon et al teaches a method for measuring a hapten that is poorly soluble in an aqueous solution such as aflatoxins (col. 2, lines 45-53). The invention permits fast, safe, and convenient measurements of haptens, which are either insoluble or unstable in aqueous solution by providing standards that are soluble and stable in aqueous solution. The standards are used to determine the amount of haptens that are present in the assay (col. 1, lines 43-48). To determine the amount of hapten in a sample, the reaction of the hapten and the antibody is compared to the reaction of the hapten-conjugate and the antibody. The conjugates of the invention are used as controls in standard immunoassay (col. 2, lines 29-40). The reactivity of the conjugate

was compared to aflatoxin standards and a standard curve was created relating aflatoxin levels to aflatoxin-conjugate levels (col. 3, lines 9-16).

It would have been obvious to one of ordinary skill in the art to use a plurality of aflatoxins in standard solutions having different known concentrations and comparing them with aflatoxin-conjugates to create a standard curve to permit fast, safe and convenient measurements of haptens. Further, one skilled in the art would know that certain levels of aflatoxins found in different amounts of grain are toxic to human and animals and a standard curve is needed to compare those levels that would be of concern.

6. Claims 11-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nasir et al in view of Dhar et al and further in view of Dixon et al.

The teachings of Nasir et al and Dhar et al are set forth above and differ from the instant claims in not teaching the assay in the form of a kit.

Dixon et al however discloses a kit for afltoxins and explains that obvious variations of preparing a kit for convenience will be apparent to those skilled in the art and points out that kits are well developed in the patent arts and literature (col. 12, lines 28-33).

It would have been prima facie obvious to one of ordinary skill in the art to take the assay for aflatoxins as taught by Dixon et al, combined with the teachings of Nasir et al and Dhar et al for the determination of mycotoxins and formulate a kit. Further, it would be convenient to do so because one can enhance sensitivity of a method by

providing reagents as a kit. In addition, the reagents in a kit are available in premeasured amounts, which eliminates the variability that can occur when performing the assay.

Response to Arguments

2. Applicant's arguments filed July 07, 2003 have been fully considered but they are not persuasive.

Applicant argue that there is no motivation to substitute the horseradish peroxidase label in the teaching of Dhar with the fluorophore taught by Nasir et al is not found persuasive.

The primary reference of Nasir et al taught a Fluorescence Polarization (FP) assay comprising mycotoxins conjugated to a fluorophore. The secondary reference of Dixon taught Applicant's particular mycotoxin (aflatoxin B1) that are detected because they are potent carcinogens found in wheat and other foods. The third reference of Dhar et al is relied on for the teaching that an aflatoxin has been conjugated in the prior art. Although Dhar et al teaches aflatoxin conjugated to a horseradish peroxidase, the primary reference of Nasir et al demonstrates that mycotoxins, which encompasses aflatoxins, can be detected in FP assays and can be conjugated to flourophore labels.

Applicant argues that Dhar et al teaches away from the instant invention because Dhar teaches a heterogeneous assay versus a homogeneous assay of the instant invention. Applicant further argues that FP assays are generally used in homogeneous assays. These arguments are not found persuasive.

The reference of Dhar et al was not relied upon for the teachings of a particular assay that teaching was provided by the primary reference of Nasir et al that taught a homogeneous FP assay. With respect to applicant's argument that FP assays are generally homogeneous is not found persuasive because FP assays does not exclude the teaching of heterogeneous assays.

Applicant's argument that Examiner has not addressed the special property of being able to bind an antibody specific for aflatoxin to produce a detectable change in FP is not found persuasive because the primary reference of Nasir et al teaches this feature (see abstract). Therefore, the prior art rejection is maintained and made final.

Conclusion

3. No claims are allowed.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A Davis whose telephone number is (703) 308-4427. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah A. Davis
CM1, 7D16
January 30, 2004

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02/02/04